PROBING NANOPARTICLE INTERACTIONS WITH BIOLOGICAL SYSTEM FOR DRUG DELIVERY APPLICATIONS

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Before any drug administered to the gastro-intestinal tract reaches the epithelium, it must traverse a layer of mucus. The main polymeric component of mucus is the glycoproteins collectively called mucins. These are complex gel-forming polymers which exhibit electrostatic, hydrophobic and H-bonding interactions and are responsible for the viscous and elastic gel-like properties of the mucus layer.

The efficacy of nanoparticles (NPs) to penetrate this layer, and deliver macromolecular drugs in therapeutic concentrations to the epithelium will depend on the surface chemistry (decoration) of the NPs. Quantifying the interactions between these NPs and the mucin gel is essential for designing successful drug delivery systems. In this project various decorations were fabricated, including zeta potential changing, slippery, and proteolytic enzymes. Figure 1 illustrates slippery and proteolytic enzyme decorated NPs penetrating a mucus layer that would stop conventional NPs.

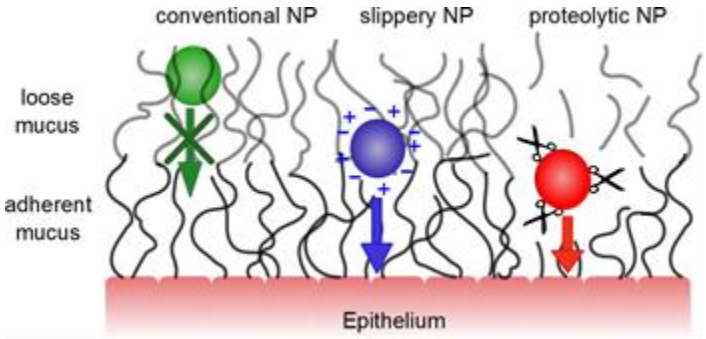

Figure 1: Possible scenarios of mucus interactions with particles of different surface chemistries

The effect of these NPs on the mobility of intestinal mucin gel was assessed by pulse-gradient-spin-echo NMR (PGSE-NMR); whereas the potential of the NPs to interact with the mucus and alter its tridimensional structure was investigated using two scattering techniques, small angle neutron scattering (SANS) and spin-echo SANS (SESANS).

The proteolytic strategy showed promising results, *i.e*. insertion of 0.5wt% of enzyme functionalized NPs to 5wt% intestinal mucin solution led to *c.a*. 2 fold increase in the mobility of the mucin molecules as measured by PGSE-NMR, this is indicative of a significant change in the structure of the mucin.
Scattering measurements also revealed a change in the mucus structure upon addition of functionalized NPs, occurring mostly at a lengthscale larger than 0.5µm.